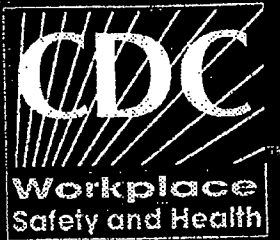


Exhibit B



Exposure Assessment Methods

Research Needs and Priorities



DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION
NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH

Exposure Assessment Methods

Research Needs and Priorities

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health

July 2002

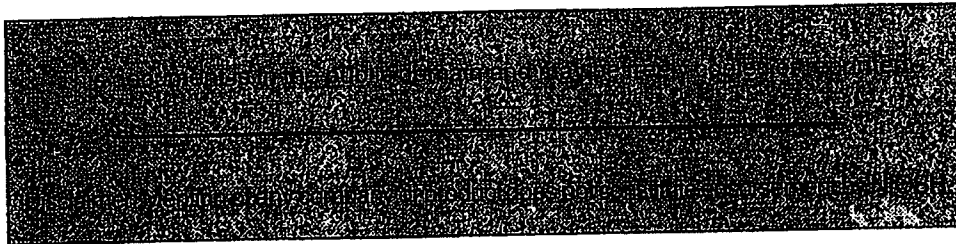


To receive documents or other information about occupational safety and health,
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In April 1996, upon the 25th anniversary of the Occupational Safety and Health Act, the National Institute for Occupational Safety and Health (NIOSH) unveiled the National Occupational Research Agenda (NORA). NORA was developed by NIOSH and approximately 500 of its partners in the public and private sectors to provide a conceptual framework to guide occupational safety and health research in the United States. This effort to guide and coordinate research nationally—not only for NIOSH, but for the entire occupational safety and health community—focuses on 21 priority areas identified as important and most likely to improve worker safety and health in the United States.

Among the 21 priority areas are eight classified as Research Tools and Approaches, including the broad area of Exposure Assessment Methods. Exposure assessment is a rapidly evolving, multidisciplinary research activity. Its purpose is to provide environmental data that can be used to: identify exposure reduction needs and methods; define exposure-response relationships in epidemiologic studies; and demonstrate the effectiveness of interventions and engineering controls. In the past 15 to 20 years, the scope of occupational exposure assessment has broadened considerably as a result of changes in technology and increased attention to nonindustrial work settings.

Implementation of NORA focuses on the formation of partnerships to assist in the development, pursuit, review, and dissemination of research for each NORA priority area. This document is a product of the NORA Exposure Assessment Methods Team—a group of individuals with a variety of backgrounds and disciplines associated with industrial hygiene, chemistry, biology, toxicology, and occupational health nursing—representing government, industry, labor, and academia. The Exposure Assessment Methods Team compiled this document in an effort to describe the research needed to advance knowledge and the state-of-the-art in exposure assessment. This document is not intended to be a definitive listing of all necessary research activities in occupational exposure assessment. Rather, the intent is to present a broader framework of the objectives and research needed to begin filling the knowledge gaps in order to further progress toward healthier workplaces and practices. Government agencies, academic institutions, public and private research organizations, labor organizations, professional societies, and others might use this document as a basis for planning and prioritizing their own research, as well as for pursuing new partnerships and identifying areas for collaborative efforts.

I encourage you to consider the research issues and needs described in this document and to join our partnership efforts to improve exposure assessment practices through research.

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APPENDIX A

ABET	Accreditation Board for Engineering and Technology
ACGIH	American Conference of Governmental Industrial Hygienists
AIHA	American Industrial Hygiene Association
BLS	Bureau of Labor Statistics
DOD	Department of Defense
DOE	Department of Energy
EA	exposure assessments
EAM	exposure assessment methods
EPA	Environmental Protection Agency
HHE	health hazard evaluations
MSHA	Mine Safety and Health Administration
NIOSH	National Institute for Occupational Safety and Health
NMAM	NIOSH Manual of Analytical Methods
NOEDB	National Occupational Exposure Database
NOES	National Occupational Exposure Survey
NOHS	National Occupational Hazard Survey
NOHSM	National Occupational Health Survey of Mining
NORA	National Occupational Research Agenda
OEDBs	occupational exposure databases
OELs	occupational exposure limits
OSHA	Occupational Safety and Health Administration
PEL	permissible exposure limit
STEL	short-term exposure limits
TWA	time-weighted averages
VOCs	volatile organic compounds



EXECUTIVE SUMMARY

The National Occupational Research Agenda (NORA) Exposure Assessment Methods (EAM) Team has proposed definitions and prioritized recommendations for research related to the field of exposure assessment. Proposed research falls into four areas: *study design*, *monitoring methods*, *applied toxicology*, and *education and communication*. The purpose of this document is to stimulate new research in these areas.

Study Design: Basic to the success of any exposure assessment is the study design and its inherent sampling strategy. Standardized data collection is a high priority, along with a practical exposure assessment guide. Research to refine job exposure matrices is needed, and a national occupational exposure survey of current conditions that will then be continually updated should be established. Another priority is a National Occupational Exposure Database (NOEDB) for storing exposure data from a diversity of sources and disseminating the data for a wide variety of research efforts. Continued research on the statistical analysis of exposure data is the final priority in the study design area.

Monitoring Methods: Measurement tools (methods and instruments) are fundamental to exposure assessment. There are three key needs in this category. The first priority is the development of guidelines for evaluating monitoring methods against standard performance criteria. The second priority topic is the development of dermal exposure assessment and biomonitoring methods. The third priority is the development of rapid, field-deployable methods.

Applied Toxicology: Understanding the underlying toxicological relationships—such as between workplace exposure and internal dose, target-organ dose, pre-clinical effects, and clinical effects—is fundamental to exposure assessment. Four recommendations are made in this area. The first calls for more mechanistic research on chemical, physical, and biological agents. The second addresses the need for a toxicity assessment protocol. The third need is for the development and evaluation of pharmacokinetic and predictive models. The fourth is a call for more research on a general toxicology approach to assess exposures to mixtures.

Education and Communication: Research scientists in exposure assessment should have knowledge of the goals and limitations of exposure assessment strategies to ensure that methods they develop and measurement data they collect are useful for risk assessment, risk management, and related research activities. Research is needed to evaluate the curricula of occupational safety and health educational programs relative to exposure assessment. Research is also needed to assess the impact on curricula of external requirements, such as those of the Accreditation Board for Engineering and Technology (ABET). The results of that research will indicate the direction to take in updating curricula and course materials so that exposure assessment methods are taught effectively. Additionally, research is needed to determine the best means of communicating exposure assessment issues and results.



In 1996, the National Institute for Occupational Safety and Health (NIOSH) and its partners unveiled the National Occupational Research Agenda (NORA), a framework to guide occupational safety and health research into the next decade. The NORA process identified 21 research priorities and resulted in the formation of partnership teams in each area. The teams—composed of NIOSH staff and professionals from other government agencies, academia, and the private sector—are developing research priorities in their focus areas. One of the NORA teams developing research priorities for the overall research agenda is the Exposure Assessment Methods (EAM) Team. Since the principal purpose of occupational exposure assessment is to protect worker health by identifying and evaluating hazards, research on exposure assessment methods is a fundamental research priority for NORA.

Occupational illnesses are an important public health issue, with an estimated 862,200 new cases occurring annually [Leigh et al. 1997]. Exposure assessment is an essential tool for understanding, managing, controlling, and reducing occupational health risks in large and small workplaces. Data from exposure assessments are used in toxicology, epidemiology, and engineering studies. While important gains have been made in creating new methods and detecting even lower exposures for some substances and agents, important challenges remain. For example, the benefits of exposure assessment are still not realized in many workplaces. Many substances, agents, and stressors lack exposure methods. Exposure data are not currently aggregated on a national basis to support improved priority setting for occupational health.

Advancing the science of exposure assessment can lead to (1) better identification of at-risk workers, (2) better identification of the most cost-effective control and intervention strategies, (3) better understanding of exposure-response relationships, and (4) improved baseline data for standard setting and risk assessment. Accordingly, the purpose of this document is to identify and promote major areas of exposure assessment methods research which, if completed, will have substantial impact on the protection of worker health. The EAM Team, receiving input from professionals across the occupational health community, identified a list of research needs regarding exposure assessment. Within this document, the needs have been grouped into four categories: Study Design, Monitoring Method Development, Applied Toxicology, and Education. The EAM Team has identified high priority items within each category.

Broad perspectives of occupational exposure assessment were discussed, including human factors and psychosocial elements. The EAM Team considered the work of others, particularly that of the American Industrial Hygiene Association (AIHA) Exposure Assessment Strategies Committee [Damiano and Mulhausen]; the American Conference of Governmental Industrial Hygienists (ACGIH)/AIHA Task Group on Occupational Exposure Databases [Lippmann 1996]; and an earlier work at NIOSH [Leidel et al. 1977]. Through discussions and evaluation of the collected information, the EAM Team discovered a lack of clarity among similar terms and a need to promote a common understanding of exposure assessment principles in this document.



Occupational exposure can be defined as the act or the condition of being subjected (as a result of work) to a chemical, physical, or biological agent, or to a specific process, practice, behavior, or work organization. *Exposure* is distinguished from *dose* in that *dose* refers to the amount of the potentially hazardous agent that is absorbed or retained by the body, while *exposure* refers to the presence of a hazard that contacts the body or is experienced by the worker.

Occupational exposure assessment is the application of a body of knowledge to determine the relevant characteristics of one or more environmental factors that pose health and safety risks to workers. In this document, while safety-related factors are covered in the course of discussion by some of the recommendations on health-related matters, the coverage of safety is not intended to be comprehensive. The authors of this document have chosen to concentrate primarily on health-related exposure assessment. The process of occupational exposure assessment includes identifying and characterizing workplace exposures; evaluating their significance; and developing estimates of exposures to individuals or groups of workers, which may be used in risk assessment or exposure-response studies. This assessment process is based on measurement and evaluation of one or more characteristics of the exposure environment and may or may not involve hypothesis testing.

Exposure assessment methods are developed by researchers from various disciplines and applied by a wide spectrum of health and safety professionals. As a result, various definitions of terms within exposure assessment—such as *hazard identification*, *exposure characterization*, *exposure evaluation*, and *exposure estimation*—have evolved and may have different meanings for different individuals working in the same field. For the purpose of this document and to promote clearer communication among the various disciplines concerned with exposure assessment, the EAM Team proposes the following definitions:

Hazard Identification: Establishing the existence of a hazard through field observations and/or laboratory analysis of the exposures and/or adverse health effects.

Exposure Characterization: Describing the qualities of a given environment. These may include the source, magnitude, frequency, duration, and routes of the exposure; the chemical and physical properties of an agent; the organizational or behavioral properties of an environment; and the potential for interaction with the human body or influence over human behavior.

Exposure Evaluation: Determining the significance of an exposure relative to known or perceived risks.

Exposure Estimation: Developing an approximate exposure value for an individual or a statistical distribution of exposure values for groups of workers in similar exposure conditions.



Thus, the occupational exposure assessment process—defined as identification, characterization, and evaluation of workplace hazards—is necessary for effective hazard surveillance, which is the ongoing systematic collection, analysis, and interpretation of exposure data essential to the planning, implementation, and evaluation of occupational health practice. Hazard surveillance, linked to medical surveillance and epidemiological and toxicological studies, provides the essential information for the exposure-response determinations and risk assessments necessary for the protection of worker health.

Recommendation: Clear communication is necessary to study, perform, and teach exposure assessment. However, the above terms and others related to them have each evolved differently within the various sectors of public health so that their meanings can be unclear. The EAM Team recommends the definitions above for general acceptance in occupational exposure assessments.



Human exposure assessment encompasses many areas from environmental quality and source emission to biological monitoring and health effects. Exposure assessments (EA) can also be made on a variety of hazards such as chemical, physical, biological, or psychosocial and can be conducted for a variety of reasons. One is hypothesis-driven to evaluate exposure-disease relationships; another involves risk assessment. The goal of exposure assessment is the same regardless of why or how the study is conducted—intervention or prevention of the exposure.

A major obstacle in exposure assessment is the lack of resources: both well-trained researchers and adequate funding are needed. Future exposure assessment activities will also benefit from multidisciplinary teams, so that the assessments are more comprehensive and better designed. Partnerships among industry, academia, labor, and government agencies—both national and international—are needed to link exposure assessment to public health practice and to leverage the necessary resources.

The goal of this document is to highlight the critical needs that must be addressed to improve key areas of exposure assessment. After defining the scope of occupational exposure assessment methods, the EAM Team brainstormed items for a comprehensive list of research needs related to EA. With input from many colleagues, the team then generated a list of 116 items that varied from broad research gaps to detailed recommendations.¹ As the list was reviewed and clarified, it became obvious that most of the items fell naturally into four distinct groupings: *Research Priorities in Study Design*, *Research Priorities in Monitoring Method Development*, *Research Priorities in Applied Toxicology*, and *Research Priorities in Education and Communication*. The team then identified high priority items from within each category and provided recommendations for each that will promote EAM research by the occupational and environmental health communities.

Research Priorities in Study Design

Basic to the success of any exposure assessment is the study design and its inherent sampling strategy. The EAM Team defines this aspect of exposure assessment as extending beyond the early phases of planning and data gathering to data analysis and interpretation, as well as to data quality assurance. A well-designed study is critical for a scientifically defensible exposure assessment that produces valid data, leads to a better understanding of disease, and results in improved public health. A poorly designed study may waste resources, produce data that are inconclusive or, even worse, lead to invalid conclusions that leave the public inadequately protected. Unfounded conclusions can also lead to unnecessary or ineffective intervention. The defense against those pitfalls is a rigorous degree of attention to study design and quality assurance.

¹The list of items is available upon request.



Many factors must be considered in the design of an exposure assessment, including but not limited to:

- The purpose of or motivation for the exposure assessment.
- Compounds, agents, processes, procedures, or behaviors to be measured.
- Availability, accuracy, precision, and practicality of sampling and analytical methods.
- Duration, type, and number of samples to be collected.
- Sampling strategy to adequately characterize (based on purpose and motive) the exposure of an individual or exposures across individuals, locations, and time.
- Duration of exposure to be characterized (acute vs. chronic, continuous vs. episodic, etc.).
- Type and extent of historical exposure information available for retrospective assessment.
- The contribution of nonoccupational exposure to aggregate exposure and cumulative exposure.
- The appropriate exposure metric and statistical descriptors to be used in relating exposure to effect.

Each of the above considerations, individually and collectively, are rich in research opportunities. The EAM Team has developed several specific recommendations and comments related to the study design of future research and has categorized them in terms of *Data Quality*, *Data Collection*, *Data Management*, and *Data Analysis*.

The primary recommendations are to support development of a practical exposure assessment guide that defines the standard practice in the field, development of new job exposure matrices, creation of an ongoing National Occupational Exposure Survey (NOES), development of a National Occupational Exposure Database (NOEDB), and updating of the NIOSH Occupational Exposure Sampling Strategy Manual.

Data Quality

Development of practical exposure assessment tools: Although related documents and publications exist, there is no single document to reference as standard practice. As a result, data are collected and maintained in a variety of ways that can be incompatible with each other. Development of a guide and a data system would ensure that consistent data are collected. Also, it is essential that collected data accurately represent workers' exposures. Accuracy may be compromised by a variety of factors. Quality assurance should be an integral part of the development, implementation, and analysis of any exposure assessment protocol. Quality could be assured in several ways, including protocol review before measurements are made, oversight during measurements, or auditing of results.



Recommendation: Develop a practical exposure assessment guide linked with matching software for managing and maintaining exposure assessment data. The guide and software should effectively serve both small and large businesses.

Data Collection

Research is needed to recommend what data should be collected and maintained by workplaces. It should lead to more standardized data collection, as well as to better baseline and background data collection efforts for physical and biological agents, biological markers, some chemicals, stressors, and human factors. The EAM Team makes two specific recommendations related to data collection:

Refinement and development of exposure matrices: Exposure matrices are datasets that provide quantitative or qualitative information about exposures as a function of industry, occupation, exposure, and circumstances of exposure. The research toward refinement and development of exposure matrices should also take into account:

- Transient, seasonal, and intermittent exposures (i.e., contract industries, construction, agriculture).
- Worker variability (intra- and inter-individual).
- Control systems in place.
- Worker demographics.
- Types of data and how it may or may not be used (qualitative, semi-quantitative, quantitative).

Recommendation: Perform research to help improve, validate, and standardize exposure matrix variables and data collection techniques. Beyond the refinement of the data collection techniques, the occupational health community needs additional exposure matrices to be defined and documented for public access.

An updated and ongoing National Occupational Exposure Survey: NIOSH conducted the National Occupational Hazard Survey (NOHS) in the early 1970s, the NOES in the early 1980s, and the National Occupational Health Survey of Mining (NOHSM) in the mid 1980s. These important studies of potential exposures among a wide variety of U.S. workers should be updated as one essential portion of the occupational health research infrastructure. The NOES has been widely used by government, academic, and private parties. However, the data are now almost 20 years old and are often questioned in light of technical and personnel changes in industry since the surveys. The EAM Team is aware that there is an initiative within NIOSH to update the NOES and encourages continued efforts in that regard. [Boiano and Hull 2001].

Recommendation: Develop innovative mechanisms for continually updating the NOES dataset. One such broad mechanism could be a series of industry-specific surveys, having a repeating cycle of every five years, perhaps. A core of information



could be obtained from all industries, but certain, more specific information could be targeted to individual industry needs, as well as to evolving needs of the research community. Other directions to consider for enhancement of an NOES include:

- Incorporation of additional descriptors of the workforce and workplace.
- Expansion to cover a wider array of U.S. workplaces.
- Expansion to cover biological, physical, ergonomic, and psychosocial hazard exposures.
- Linkage of the NOES data with complementary and supplementary data from other sources.
- Updated data recording, processing, and dissemination strategies.
- Development of consensus standards for data formats to ease exchange and analysis.

Data Management

A National Occupational Exposure Database: An NOEDB has been suggested and encouraged in recent years by a number of parties (e.g., NIOSH, Department of Defense, Department of Energy, Environmental Protection Agency, and AIHA). The NOEDB would meld, store, and disperse exposure data from a wide variety of sources—general and specific exposure matrices; the NOES, Occupational Safety and Health Administration (OSHA), and Mine Safety and Health Administration (MSHA) compliance data; and isolated industry-occupation specific sets of exposure data. Such a database would allow the establishment of exposure profiles for industries, processes, jobs, tasks, and similar strata. The design, implementation, and maintenance of an NOEDB would necessitate more exposure assessments and spur the development of new, faster, cheaper, and better sampling methods. It would provide a source for industry census-type data and better quantification of exposures. When linked with a national occupational health surveillance system or Bureau of Labor Statistics (BLS) surveys, the NOEDB would be an ideal source of information for epidemiologic studies, risk assessment, risk management, and development of occupational exposure limits (OELs).

As with the NOES, the NOEDB may be viewed as an essential part of the infrastructure needed for a rational program of occupational health protection, promotion, and research. While NIOSH may be one of the few organizations well-suited to establish and maintain a NOEDB, collaborators would be needed. OSHA, MSHA, BLS, and other organizations in the private and public sectors would be logical contributors. As a non-regulatory agency with a national mission, NIOSH is uniquely positioned to collect and manage the data, which could be contributed by a wide variety of parties. NIOSH could enter its own data from health hazard evaluations (HHEs) and other surveys. Other agencies (federal and otherwise) and private organizations could also submit data. The protection of personal and company identifiers would have to be assured, while identification of crucial cell descriptors was maintained, e.g., industry, occupation, controls present, and analytical technique. Data integrity would need to be addressed as well.

Recommendation: Create a NOEDB. Thoughtful, creative design work is needed before an NOEDB could be implemented. This work would address such issues as data integrity, Internet access, search and retrieval software, hardware specifications, and links to other



databases (e.g., employment or medical surveillance). The details of designing such a program are beyond the scope of the EAM Team and should most likely be undertaken by a NIOSH-OSHA-stakeholders team. Research grants and cooperative agreements could be used to identify and evaluate different models to determine at least one feasible design.

In this area, there are several examples of previous and ongoing work: the ACGIH-AIHA Task Group on Occupational Exposure Databases (OEDBs) has published recommendations for airborne hazards and noise [2001]; the Department of Defense (DOD) is currently working to coordinate and link all of its OEDBs; the Department of Energy (DOE) has a centralized database on radiation exposure and is establishing one for beryllium; NIOSH, along with the Ford Motor Company and other partners, has been developing the HEAR-SAFE database on noise-related hearing loss; and NIOSH is pilot testing an industrial hygiene data management system for use with retrospective occupational exposure assessments.

Data Analysis

Research is encouraged regarding statistical methods applied to sampling strategies and related exposure assessment issues. The EAM Team has identified several specific topics that need further research and support, particularly for developing the following tools:

- Qualitative, semi-quantitative, and quantitative exposure prediction techniques and models.
- Validation techniques that determine the accuracy and precision of the measures and models.
- Modeling strategies and statistical methods for reaping benefits, when appropriate, of real-time data collection rather than modifying the data to fit methods for short-term exposure limits (STEL) or time-weighted averages (TWA) analyses.
- Methods to balance the classically defined adequate sample size with logistics and of feasibility often found in small-scale plant operations.
- Strategies to collect and use representative data from small or transient operations and/or businesses (especially where adequate exposure data are not available), such as the development of experimental design approaches where individual factors are identified and varied using a multi-factorial design.

The *NIOSH Occupational Exposure Sampling Strategy Manual* [DHEW (NIOSH) 77-173] needs to be updated. This need is due in part to the extensive development of statistical methods for occupational exposure assessment since the first publication of the *Manual*. The 1977 *NIOSH Manual* prescribed specific procedures for collecting, analyzing (statistically), and interpreting exposure data relative to the OSHA permissible exposure limits (PELs). These procedures were intentionally designed to provide the employer with a means of rapidly determining that the work environment was acceptable. The presumption was that exposures were already controlled and the employer only needed an objective yet quick and resource-efficient means of demonstrating compliance. A new guide is needed to assist employers in designing site-specific, efficient, and effective exposure assessment programs, which consist of problem definition, data collection, data analysis, and data interpretation elements. The presumption should be that exposures may



not be controlled and that a properly designed program will have a high likelihood of detecting a poorly controlled work environment.

Recommendation: Develop an exposure data interpretation and analysis guide. The document should provide guidance regarding (1) the degree of statistical rigor needed in the range of circumstances that confront practicing industrial hygienists, (2) the design of performance-oriented exposure assessment strategies, (3) predictive techniques, and (4) models. Such performance-oriented strategies could be site-specific, reflecting the available resources, but designed so that the risk management goal inherent in federal and consensus exposure limits is realized. The updated document should recognize the need for pragmatic approaches when statistical rigor cannot be attained. It is possible, for example, that a hierarchical logic for statistical testing could provide occupational health professionals with straightforward, practical guidance for exposure assessment strategies. Research and validation studies would be needed for these pragmatic approaches.

Recommendation: Develop qualitative, semi-quantitative, and quantitative predictive techniques and models.

Other Study Design Research Items

The EAM Team determined that data quality, collection, management, and analysis were the major types of research needs related to study design, but many other items were also recognized. Other important items suitable for research support (but listed in no particular order) include:

- Standardized procedures for characterizing individual work practices and tasks, such as real-time video exposure monitoring, personal telemetry, or field-portable data recorders.
- Research into the role that worker activity plays on the routes of exposure and the mechanisms of uptake.
- Research to better determine how to relate fixed-location measurements to personal exposure.
- Research concerning the interactions of chemical, biological, and physical exposures with stress, behavioral aspects, circadian rhythms, and other psychosocial exposures.
- Guidance and recommendations on using questionnaire instruments and data for exposure assessment, particularly with respect to cross-validation of physical assessments in the work environment.
- Research regarding the best means of disseminating the results of exposure assessments—an area that is also addressed in the Education and Communication section of this paper.
- Research regarding biomarker exposure assessment studies, including determination of the most effective methods for soliciting participation, establishing the marker's validity, and interpreting and communicating the results.
- Enhanced methods for historical exposure reconstruction.



- Standardized methods for ensuring the accuracy of results, such as occasional audits, because the circumstances of measuring exposures can influence results.
- Research to determine the appropriate study designs for assessment of mixed exposures, as well as their combined health effects. The NORA Mixed Exposures Team is addressing research needs in this area.

Research Priorities in Monitoring Method Development

Measurement tools (methods and instruments) are fundamental to exposure assessment. Various tools are specific to the different exposure assessment disciplines (environmental, biological, psychosocial, and ergonomic). Ideally, all methods should be evaluated and validated for their intended use and should be performed by qualified practitioners who are certified or accredited.

Method Guidelines

Highest priority is given to producing guidelines for development and evaluation of measurement methods. Guideline documents are needed that address dermal exposures, biological monitoring methods, measurements made using direct-reading instruments, data-logging monitors, and diffusive samplers.

These guidance documents would be similar to *Guidelines for Air Sampling and Analytical Method Development and Evaluation* [Kennedy et al. 1995]. Such guidance specifies the experimentation required for determining method performance, primarily accuracy, but also precision, sample stability, limit of detection, and others. The new guidance would also specify the experimentation needed to verify performance (accuracy) under the extremes of conditions possible in the field and/or laboratory. Finally, the guidance would specify the calculations needed and the criteria to be met. Where applicable, the target criterion for accuracy used by NIOSH and OSHA (95% confidence that results are within 25% of the true value 95/100 times) would be incorporated, although techniques not meeting this criterion might still be useful.

Recommendation: Produce guidance documents for the development and evaluation of monitoring methods that use direct-reading instruments, data loggers, or diffusive samplers; for dermal-exposure monitoring methods; and for biological monitoring methods.

Biomonitoring Methods Research

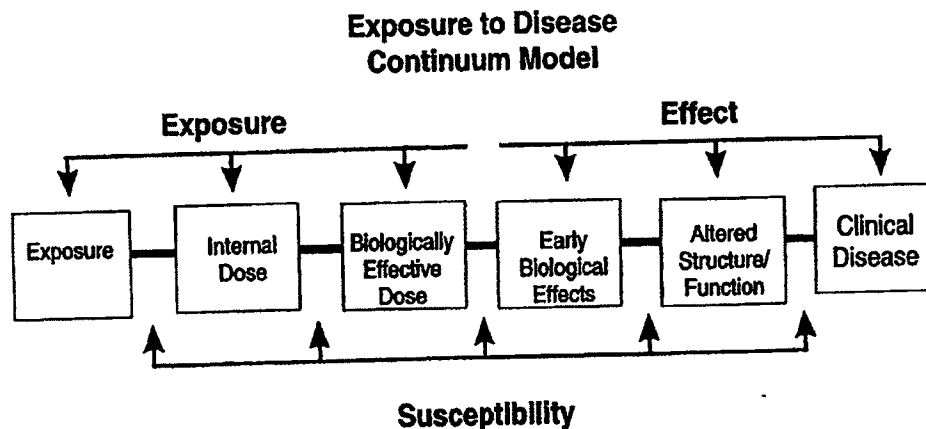
Traditionally, occupational exposure assessments have focused on airborne exposures in the workplace. Biomarkers of exposures, such as chemicals and their metabolites, can be used to complement traditional environmental monitoring, especially with agents having multiple routes



of entry. Biomarkers can provide important confirmation when an exposure is difficult to measure directly in the work environment. This situation includes episodic and random exposures. Biomarkers can also provide information on the biological effects of exposure and the effectiveness of controls, as well as an individual's susceptibility to both exposures and effects (Figure 1). Some biomarkers of effect can serve as early indicators for disease risk. In short, biomarkers offer the potential to accomplish more integrated exposure assessments.

Research and development of biomonitoring techniques will help improve exposure assessments and knowledge of the relationship between exposure and disease risk. Because of biological and work practice differences, workers may receive various internal doses even though their occupational environment via traditional air monitoring appears to be the same. Due to the actual differences in exposures and possible differences in susceptibility, these workers can be potentially at very different levels of risk. Biomonitoring techniques are important because they can

Figure 1



Adapted from Schulte PA (1993). A Conceptual and Historical Framework for Molecular Epidemiology. In: *Molecular Epidemiology Principles and Practices*. Ed., Schulte PA and Perera FP. Academic Press, San Diego.



measure the internal dose of an agent from all routes and all sources of exposure and have the potential to better classify risk. Biomarkers of exposure should provide quantitative data on the extent of exposure and be suitably selective for the application. Biomonitoring methods may include abnormal rates of normal processes, e.g., cardiovascular measures.

Recommendation: Develop and validate biomonitoring methods to assess the internal and biologically effective dose of an occupational exposure.

Recommendation: Perform more research to provide and characterize the performance (specificity, sensitivity, accuracy, etc.) of exposure biomarkers and their relationship to external measurements of potential exposure.

To better understand the link between exposure and disease, new biomonitoring methods are needed. Adverse effects are usually reversible if detected early. Markers of these early adverse effects are, thus, important for guiding intervention. Although biomarkers of effect may show that exposure has occurred, they may not provide insight into the nature and magnitude of that exposure. For example, sister chromatid exchanges indicate an effect, yet may be caused by many different toxic agents having poorly understood dose-response characteristics.

Recommendations: Develop new, validated biomarkers.

Markers of susceptibility, while just beginning to be researched, also offer potential for preventive intervention. There is substantial variability in biological response to environmental agents. Susceptibility markers can be a whole host of factors, ranging from genetics, diet, and metabolic rate to repair mechanisms.

Recommendation: Perform more research on factors that may affect host susceptibility and risk of disease.

NIOSH currently publishes the *NIOSH Manual of Analytical Methods* (NMAM) for detection of environmental chemicals. NMAM is useful because occupational safety and health practitioners have standardized methods. Occupational safety and health practitioners would benefit from a comparable set of validated, standardized biomonitoring methods.

Recommendation: Publish biomonitoring methods as a companion to, or part of, the NMAM.

As biomonitoring methods are developed, the ethical, legal, and social issues related to these advances need to be addressed. These are critical issues that need to be resolved before biomarkers can be fully used in occupational safety and health practice. The potential for unethical use of biomarkers is great, perhaps more so for susceptibility markers that may be used in discriminatory practices. A major issue is what to do with employees who have altered biomarker results in the absence of disease [Ashford et al. 1990].



Recommendation: Perform research and engender dialogue to help resolve the ethical, legal, and social issues of biomonitoring.

Dermal Exposure Measurement Methods

The skin is a complex organ through which some compounds pass more readily than others. Dermal exposure cannot be estimated from measurement of airborne concentrations. Improved techniques for dermal exposure assessment are important to help assess that route's contribution to total exposure. Dermal exposure assessments can also help evaluate the efficiency of personal protective clothing performance. Although biological monitoring is often an important technique in assessing dermal exposure, biological monitoring methods are not always available. Thus, more direct dermal exposure techniques are needed. Such techniques might also identify exposed skin areas so that intervention is effective. Research is also needed to ascertain factors that may affect the skin absorption rates. The Allergic and Irritant Dermatitis NORA Team is also looking at this issue and will have more specific recommendations.

Recommendation: Substantially increase research on dermal absorption and dermal exposure assessment methods.

New Environmental Monitoring Methods

Research is encouraged that leads to new or improved measurement methods. New methods would measure workplace hazards that could not previously be measured. Improved methods would be capable of making measurements more accurately, more quickly, or less expensively.

Exposure to chemicals is widespread in the workplace. New field-readable methods for monitoring exposure to chemicals are encouraged because they are usually both quicker and less expensive, even though some results from the field may need to be verified by laboratory measurement. Improved real-time monitoring methods are needed that are capable of accurately determining short-term exposures, exposures to ceiling values, and the efficacy of engineering controls. Finally, methods that address multiple analytes at low levels are encouraged, e.g., isocyanates or volatile organic compounds (VOCs). Although research into all these areas needs to be supported, no particular chemical hazard or measurement technology can be singled out as a dominant need for the future.

Recommendation: Develop and evaluate new or improved methods for assessing exposure to workplace chemicals. Methods that are field-deployable, measure low concentrations, or measure multiple analytes are especially encouraged.



Exposure to microorganisms or their byproducts in the workplace is of increasing concern, but methods of assessing that exposure are not well defined. Thus, evaluated, sensitive, and specific methods are needed for assessing exposure to microbes and microbial toxins, including non-aerosolized microbes, bioaerosols, and bioaerosol mixtures. Methods should include nonculturing approaches, for example DNA amplification and comparison to methods based on culturing as needed.

Recommendation: Develop and evaluate new methods for assessing exposure to workplace microbial contamination.

Exposures to physical agents are found in many workplaces and are changing as the result of new technologies. While monitoring methods are well developed for some physical agents, monitoring research is needed for new technologies (e.g., time-domain voice and data transmission), as well as for some familiar agents that pose scientific challenges. Methods are needed for various forms of electromagnetic radiation, heat, noise, vibration, and high-speed particles.

Recommendation: Develop and evaluate new or improved methods for assessing exposure to physical hazards in the workplace.

Research Priorities in Applied Toxicology

Applied toxicology is a key component of hazard identification and exposure evaluation. In some cases, the exact toxicological agent in a workplace exposure has yet to be identified; exposure assessment is most effective when the toxicology is fully understood. Understanding the underlying toxicological relationships, such as between workplace exposure and internal dose, target-organ dose, pre-clinical effects, and clinical effects, is fundamental to exposure assessment.

Applied toxicology does more than identify hazards; more importantly, it elucidates mechanisms of toxicity, which provide the information essential in the design of exposure assessment and intervention strategies. Some of the research needs in biomonitoring overlap those of applied toxicology.

Research is needed not only to identify toxicological hazards but also to discern the mechanism of toxicity. This information is needed to allow the development of biomarkers and aid in the interpretation of the results. Dosimetric models are also needed to extrapolate laboratory findings on mechanisms to the human body and the more complex exposures found in workplaces. Such research can produce exposure metrics, which are more closely related to the biologically effective dose and disease risk. Information can be obtained that is useful for monitoring workers' exposures or implementing intervention strategies.

Recommendation: Perform more research to ascertain the mechanism of action for chemicals and for physical and biological agents.



The development of a generalized protocol for rapid assessment of toxicology is encouraged. This would entail research to determine what basic data elements are needed to make a preliminary assessment of toxicology for a new agent. It would lead to a practical document containing toxicological data and a protocol so that field personnel could determine the appropriate exposure assessment method, levels of control (engineering, personal protective equipment) and medical surveillance.

Recommendation: Develop a toxicity assessment protocol, including guidelines for a systematic approach to estimating occupational exposure limits.

Pharmacokinetic models are important to ascertain dose-response relationships, particularly if the results can be applied to more than one agent. Modeling is also needed to assess internal dose because it is critical to know when to conduct environmental monitoring or sampling of biomarkers. This is especially important for agents that are stored internally or have delayed toxic effects. For example, if the agent is rapidly excreted, analyzing urine 48 hours after exposure is not a good use of resources. Use of human exposure assessment data in pharmacokinetic modeling will help to establish the link between exposure and disease.

In addition to pharmacokinetic modeling, other types of modeling systems are important. Models that predict toxicity based on chemical structure show great promise and could be user friendly. Predictive models have the potential to help design better exposure assessment tools.

Recommendation: Develop and evaluate pharmacokinetic and predictive models of toxicity.

Determining the toxicologic effects of mixtures is an important research area. Exposure to a single agent is rare in an occupational setting. Rather, it is a mixture of exposures that may act antagonistically, synergistically, or additively. Development of accepted mixture exposure assessment methods are needed to support occupational exposure limits. The NORA Mixed Exposures Team is addressing this topic and will have specific recommendations.

Recommendation: Perform more research to develop a general applied toxicology approach to assess exposure to mixtures.

Research Priorities in Education and Communication

Exposure assessment is a primary mechanism that drives decision-making in the prevention of occupational illness. It is imperative that research scientists in exposure assessment have knowledge of the goals and limitations of exposure assessment strategies to ensure that the methods they develop and measurement data they collect are useful for risk assessment, risk management, and related research activities. Exposure assessment research professionals, because they are educated in a variety of disciplines, would benefit from additional knowledge of work environments, exposure



assessment strategies, and some underlying principles of public health. Such content should include an understanding of the following: sources for workplace hazards, exposure magnitude and variance over time and space, the dynamic nature of chronic diseases in populations, and appropriate analytical approaches for estimating rates and risks in populations. These professionals would then have the ability and interest to collect appropriate data and conduct the research needed to improve worker health while also advancing the science of exposure assessment. Clear communication of exposure assessment principles to broad segments of the public is an important skill for professionals.

Specific knowledge in the following areas is needed to estimate worker exposures and should be considered as elements in advanced exposure assessment curricula:

- Principal factors that cause or modify worker exposures to chemical, physical, and biological agents.
- Rationale and approaches for both formal and informal study designs since the purpose of exposure monitoring and data collection affects the types and quality of the measurement data.
- Appropriate exposure assessment methods, as discussed in the previous sections, to identify and characterize the magnitude and variability of exposures in groups of workers.
- Statistical measures used with exposure assessment data either to perform or assist in the completion of the appropriate analysis.
- Standard terminology, such as chemical nomenclature, physiologic response, and environmental conditions, to clearly communicate exposure assessment concepts.
- Skills to communicate exposure assessment results and their implications for worker and public health to a variety of audiences.
- Appreciation of the social, ethical, and legal dimensions of exposure assessment.

Most curricula require various courses where basic and advanced principles of these elements are emphasized. Rarely, though, are courses offered that integrate this knowledge to ensure appropriate design and selection of exposure assessment strategies. As a result, what data are collected have limited utility for important exposure assessment analysis and larger worker health studies.

Recommendation: Inventory the content of existing curricula to assess inclusion and integration of specific knowledge elements needed for exposure assessment. Determine whether the elements covered have an impact on practice.

Curriculum requirements (ABET, etc.) need to be examined to determine their appropriate role in setting curricula in exposure assessment.

Recommendation: Compare requirements for industrial hygiene education program content for ABET and other accreditations to determine if a unified set of requirements or guidelines can be established and make recommendations to appropriate accrediting bodies.



Identifying the necessary elements of an exposure assessment education does not necessarily mean that professionals will be supplied with all relevant information. Practical and theoretical reference materials should be emphasized as necessary. Lastly, continuing professional education is important to ensure that research findings and new technology are readily transferred to practicing professionals and research scientists.

Not only is it important that the key elements for exposure assessment education be determined but also effective communication methods for exposure assessment research results should be identified and taught. Clear communications are required to have a significant impact on professional colleagues, as well as on the public health and public policy communities.

Recommendation: Identify and develop effective methods for communication of exposure assessment elements, study design, monitoring methods, results, conclusions, and recommendations. Consideration of various audiences is necessary, as communication methods may vary in their effectiveness for reaching different audiences, such as public health professionals, workers, and policy makers.



Summary

The goal of NORA activities is to determine the research priorities for the nation in the field of occupational safety and health and to advance that research where possible. Twenty-one broad research areas were identified when NORA began, and teams were assembled for each of those.

The NORA EAM Team, as are other NORA teams, is made up of NIOSH researchers and persons representing industry, academia, labor, and other government agencies. The team brainstormed research needs in the field of exposure assessment methods. The team also consulted with many other researchers and other professionals in industrial hygiene. Given this input, the team then prioritized the research needs and in the process grouped them into four categories.

The recommendations of the team fall into the four areas: *study design*, *monitoring methods*, *applied toxicology*, and *education*. The first two—study design and monitoring methods—are the most germane to the topic of exposure assessment and abound with research opportunities. However, the impact of applied toxicology and education and communication activities on exposure assessment activities are too important to ignore. Specific recommendations are spelled out in this paper.

This paper is not a one-time effort. The process of identifying research priorities and seeking avenues for accomplishing that research will be ongoing. Therefore, the NORA EAM Team invites comments and dialog from interested parties.



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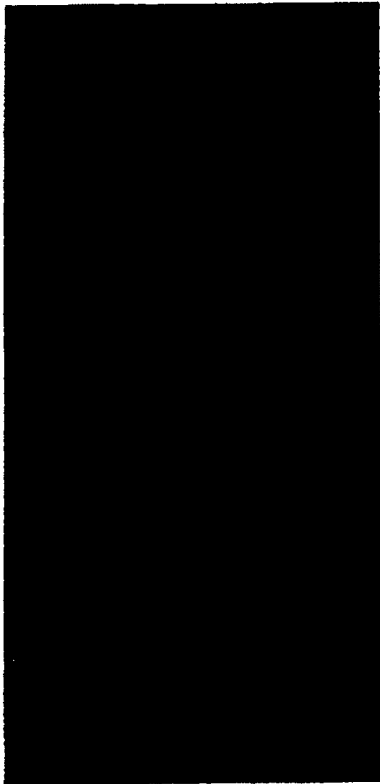
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